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## DETAILED DESCRIPTION

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[Detailed Description of the Invention]

[0001]

[Industrial Application]This invention relates to the high medical-application fats-and-oils containing composition of the effect which reduces the neutral lipid and the cholesterol content in blood, and controls a platelet aggregation activity.

[0002]

[Description of the Prior Art]In recent years, the hyperlipidemia disease with high neutral lipid (triglyceride) in blood and value of cholesterol is increasing by making diversification of an eating-habits style, the excess of ingested calories, and other factors into a background. Hyperlipidemia is considered to be the risk factor which causes condition, such as ischemic heart disease and arteriosclerosis, soon.

[0003]Positive correlation is accepted between the cholesterol count in a blood serum, and the onset percentage of risk of ischemic heart disease, If the cholesterol count in a blood serum is reduced, it is made clear from the result of epidemiological survey that the onset percentage of risk of ischemic heart disease also falls (for example, MIZUSHIMA, Yutaka et al., "today's remedy (1993 editions)", the 361st page, Nankodo). The hypertriglyceridemia is connected with the onset of a fatty liver, pancreatitis, etc., and also the side as risk factor of ischemic heart disease is pointed out. Therefore, hypercholesterolemia and the hypertriglyceridemia pose a big problem also in hyperlipidemia especially clinically, and, generally to a hyperlipemic subject as this measure with alimentary therapy, such as ingested-calories restrictions. The therapy by administration of antilipemics, such as clofibrate, nicotinic acid cholestyramine, tocopherol nicotinate, soysterol, and dextran sulfate, is performed.

[0004]Also in arteriosclerosis, fatty deposition and plaque formation happen to intimae, such as coronary arteries, a basilar artery, a renal artery, a breast, an abdominal aorta, and atherosclerosis is considered to be the origin with big unusual accumulation of lipid, such as a

fat in a blood vessel wall, and cholesterol. In arteriosclerosis, adhesion and an aggregation of blood platelets are conjointly promoted with the abnormalities of a blood vessel wall, and the abnormalities of a blood flow, and it goes on to an arterial thrombus soon. The thrombolytic agents (for example, urokinase, streptokinase, etc.) for dissolving the antiplatelet therapy which makes a subject platelet aggregation depressants (for example, awrfarin, aspirin, etc.), and the thrombus and plug which were done are widely used for the therapy of the arterial thrombus using a drug.

[0005]What has a platelet aggregation operation and a vasoconstrictor action in eicosanoids compounded from polyunsaturated fatty acid in the living body, such as a prostaglandin and thromboxane, Conversely, it turns out that there are some which have platelet aggregation depressant action and vasodilatation, and these eicosanoids are closely involved with the onset of arteriosclerosis. Also in eicosanoid, prostaglandin  $I_2$ . (it may abbreviate to  $PGI_2$  hereafter.) -- it is known that have platelet aggregation depressant action, vasodilatation, and a blood pressure fell operation, and thromboxane  $A_2$  (it may abbreviate to  $TXA_2$  hereafter.) has a platelet aggregation induction operation and a vasoconstrictor action.

[0006]Thus, if the concentration of cholesterol in the lipid concentration division blood in blood and triglyceride in blood becomes high, the symptoms of hyperlipidemia will be shown, This causes condition, such as ischemic heart disease, soon, and when the lipid in blood carries out unusual accumulation at a blood vessel wall, adhesion and an aggregation of blood platelets will be promoted, And it is known that lead to formation of an arterial thrombus, it is said that condition, such as atherosclerosis, will be caused, and the lipid concentration in blood has hyperlipidemia, ischemic heart disease and the cohesiveness of blood platelets and an arteriosclerosis disease, arterial-thrombus formation, etc. and close relevance.

[0007]By the way, the thing containing the ingredient for which the concentration of cholesterol in blood or triglyceride in blood is reduced is in the raw material with which the usual meal is presented. For example, said soysterol is sterol of the unsaponifiable matter contained in a soybean, and the lignan compound of sesame oil origin in JP,H3-53866,A is indicated, and ingesta which blended this, such as butter and mayonnaise, are proposed. Eicosapentaenoic acid (the number after  $C_{20:5}$ , however C expresses the number of total carbon number:double bonds.) It is the same as that of the following. All the \*\*\*\*- 5, 8, 11, and 14 and 17-eicosapentaenoic acid, it abbreviates to EPA below -- docosahexaenoic acid ( $C_{22:6}$ , all the \*\*\*\*- 4, 7, 10, 13, and 16, and 19-) [ docosahexaenoic acid and ] It omits the following DHA. it is also clear by the animal experiment or the clinical experiment that there is an operation the food material [ like ] which contains long chain polyunsaturated fatty acid and these n-3 system reduces [ operation ] the cholesterol count and triglyceride value in a blood serum (Robinson, D.R. et al. [ for example, ].) J. Lipid Res., the 34th volume, the 1435th page, 1993.

[0008]The action mechanism of a fall of the cholesterol count in a blood serum started by taking in or prescribing EPA and DHA for the patient, The cholesterol synthesis ability within liver is controlled by incorporation of the fats and oils etc. which contain long chain polyunsaturated fatty acid or this n-3 system, It is presumed because discharge of cholesterol to the inside of blood is controlled as the result (Choi, Y.S. et al., Lipids, the 24th volume, the 45th page, 1989). It is guessed that the fall of the triglyceride value in a blood serum is what is depended on long chain polyunsaturated fatty acid controlling the triglyceride composition ability in liver n-3 system (original Kenji, "fats and oils", the 46th volume, No. 4, the 90th page, 1993).

[0009]Things for which long chain polyunsaturated fatty acid inhibits a platelet aggregation operation n-3 system, such as EPA and DHA, are also known. By epidemiological survey, n-3 system Namely, ingestion of long chain polyunsaturated fatty acid and platelet aggregation activity control, It is reported that significant correlation is accepted between the falls of whole blood viscosity, and decline in the mortality rate by negative correlation or this disease is accepted between the mortality rate by the cardio-vascular system disease or a cerebral blood vessel system disease (Hirai, A. et al., Lancet, the 2nd volume, the 1132nd page, 1980). As a mechanism of the mortality decline of the ischemic-heart-disease origin by ingestion of long chain polyunsaturated fatty acid, an anti-platelet aggregation operation, a plasma lipid improving action, etc. can be considered n-3 system.

[0010]Then, in order to reduce a blood cholesterol level and the triglyceride value in blood, Or aim to prevent hyperlipidemia or to improve a hyperlipemic subject's lipid concentration in blood, in order to make platelet aggregation control, and it is aimed at prevention and the therapy of arteriosclerosis further again, The foodstuffs containing many fish containing EPA or DHA are taken in intentionally, or special formula powdered milk for puericulture, health food, etc. made from fish oil containing EPA and DHA, a fish oil concentrate, etc. are marketed. However, it is said that it is necessary to take in or prescribe these for the patient over a large quantity and a long period of time.

[0011]Although sardine oil, cod liver oil, herring oil, a cuttlefish oil, a tuna eye socket oil, etc. are mainly used as fish oil which contains long chain polyunsaturated fatty acid n-3 system, such as EPA and DHA, More than 50 mol % of the total amount of the n-3 system long chain polyunsaturated fatty acid which carries out the ester bond of each chemical structure of these fats and oils to triglyceride, and exists is used as the constituent fatty acids of the 2nd place of triglyceride, If it puts in another way, long chain polyunsaturated fatty acid has structure which carried out many ester bonds by the 2nd place rather than the 1st place of triglyceride, and the 3rd place n-3 system.

[0012]On the other hand, EPA and n-3 system long chain polyunsaturated fatty acid like DHA, While it has the reduction effect of the lipid in blood, the depressor effect of a platelet

aggregation activity, etc. as mentioned above, if it is easy to oxidize since it has many double bonds in intramolecular compared with usual, for example, edible-plants fats and oils, structural fat acid, and it takes in superfluously, bringing about a harmful operation to a living body is also known. If the hyperoxidation reaction of lipid advances in the living body, an obstacle is produced in a biomembrane and becoming a cause of lesions, such as ischemic heart disease, arteriosclerosis, a cataract, cancer, an Alzheimer disease, a collagen disease, and amyloidosis, is guessed.

[0013]By the way, if the symptoms of hyperlipidemia are shown in many cases as secondary diseases, such as nephrotic syndrome, an obstructive biliary disease, a hypothyroidism, and diabetes mellitus, and condition of disease becomes serious also in arteriosclerosis, a patient's anorexia and the fall of a digestion function will take place like the case of other illnesses. In order to cope with such a condition and to perform a nutrition or calorie supply in Medical Science Division, means, such as liquid food, an infusion solution, and lipid microsphere, are adopted.

[0014]Liquid food is a dietetic food which has the good slaking property and absorptivity corresponding to the patient in a poor nutritional condition or a digestion depression state, and little mechanical stimulus to the alimentary canal by slaking residue and which can apply to each symptoms. Although taken in in taking orally in many cases, depending on a patient's condition, an enteral target may be medicated with liquid food by an intubation. There are a natural high density liquid diet, half-digestion, a elemental diet, etc. in liquid food, and the raw material is cereals, potatoes, legumes, an egg, cow's milk and dairy products, greenstuff, fruits, marine products and meat, butter, vegetable oil and fat, sugar, etc.

[0015]An infusion solution is used for correction of the balance of nutrition maintenance when an ingestion and just administration are insufficient, moisture, an electrolyte, etc., etc., and the purpose of maintenance and maintenance of circulating blood volume, when an ingestion cannot be carried out. There are sugar transfusions, amino acid transfusions, and lipid microsphere in an infusion-of-nutrient agent.

[0016]Lipid microsphere is constituted including triglyceride, phospholipid, glycerin, etc. An amount of energy is high and has the feature of not starting the osmotic diuresis unlike sugar transfusions. In the case of an intravenous hyperalimentation therapy, it mixes with the basic liquid for intravenous hyperalimentation, and the lipid microsphere used for nutrition maintenance is prescribed for the patient from a peripheral vein so that it may mainly become about 10% of all the administration caloric content for the purpose of supply of an energy source and essential fatty acid (linolic acid etc.).

[0017]

[Problem to be solved by the invention]The place which this invention is made in view of such the actual condition, and is made into the purpose, There are no side effects to an animal

including Homo sapiens, and it is in providing the high medical-application fats-and-oils containing composition of the conventional effect which decreases the lipid concentration in blood and controls a platelet aggregation activity by a little use rather than a long chain polyunsaturated-fatty-acid supply source n-3 system.

[0018]

[Means for solving problem]In order that this invention persons may attain the above-mentioned purpose, as a result of inquiring wholeheartedly, the fats and oils in which a lot of long chain polyunsaturated fatty acid is distributed over the 1st place of glyceride structure, and/or the 3rd place n-3 system, It compares with common n-3 system long chain polyunsaturated-fatty-acid supply sources, such as fish oil in which a lot of long chain polyunsaturated fatty acid is distributed over the 2nd place of glyceride structure n-3 system, the effect of reducing a blood cholesterol level and/or the triglyceride value in blood was very high, and the effect which controls a platelet aggregation activity again was notably large, and it found out that the above-mentioned purpose was attained. This invention is completed based on this knowledge.

[0019]Namely, the summary of this invention contains long chain polyunsaturated fatty acid n-3 system as constituent fatty acids of glyceride, It is the medical-application fats-and-oils containing composition which blended the fats and oils containing the fats and oils or this mixed triglyceride which consists of mixed triglyceride which less than [ of the total amount of long chain polyunsaturated fatty acid / 40 mol % ] combined with the 2nd place of glyceride n-3 system.

[0020]In the triglyceride which comprises fatty acid in which the mixed triglyceride by which it is characterized by this invention contains long chain polyunsaturated fatty acid n-3 system, and glycerin, When the total amount of long chain polyunsaturated fatty acid is made into 100-mol % n-3 system, arbitrary fatty acid other than long chain polyunsaturated fatty acid is carrying out the ester bond to less than [ the / 40 mol % ] n-3 system at the 2nd place of triglyceride, And arbitrary fatty acid other than long chain polyunsaturated fatty acid is distributed [ n-3 system ] at random or un-at random in the 1st place of triglyceride, and the 3rd place n-3 system with more than 60 mol % of long chain polyunsaturated fatty acid, and the ester bond is carried out.

[0021]The long chain polyunsaturated fatty acid refers to the n-3 system straight-chain-shape unsaturated fatty acid in which a carbon number has three or more double bonds or more by 18 here n-3 system, concrete -- alpha-linoleic acid ( $C_{18:3}$ ) and octadeca tetraenoic acid ( $C_{18:4}$ ), 6,9,12, 15-octadecatetraenoic acid, Arachidonic acid ( $C_{20:4}$ ), EPA ( $C_{20:5}$ ), docosapentaenoic acid ( $C_{22:5}$ , 7, 10, 13 and 16, 19-docosapentaenoic acid), DHA ( $C_{22:6}$ ), etc. can be illustrated. The mixed fatty acid of one sort or two sorts or more of arbitrary rates

chosen from the group which consists of alpha-linoleic acid, arachidonic acid, EPA, docosapentaenoic acid, and DHA among these in this invention is preferred, and EPA and/or DHA are still more preferred.

[0022]Although it can be used as fatty acid other than long chain polyunsaturated fatty acid n-3 system regardless of any of short chain, inside chain, and long chain each fatty acid, saturation, and unsaturation each fatty acid, it is straight chain shape, and while a carbon number is six or more, a thing belonging to a chain thru/or long-chain saturation, or unsaturated fatty acid is desirable. As this fatty acid, caproic acid ( $C_{6:0}$ ), caprylic acid ( $C_{8:0}$ ), Capric acid ( $C_{10:0}$ ), lauric acid ( $C_{12:0}$ ), myristic acid ( $C_{14:0}$ ), Pulmitic acid ( $C_{16:0}$ ), palmitoleic acid ( $C_{16:1}$ ), Stearic acid ( $C_{18:0}$ ), oleic acid ( $C_{18:1}$ ), Elaidic acid ( $C_{18:1}$ ), linolic acid ( $C_{18:2}$ ), alpha'-linolenic acid ( $C_{18:3}$ , 5,8,11-octadecatrienoic acid), Gamma-linolenic acid ( $C_{18:3}$ , 6,9,12-octadecatrienoic acid), Eleostearic acid ( $C_{18:3}$ , 9,11,13-octadecatrienoic acid), Arachidic acid ( $C_{20:0}$ ), gadoleic acid ( $C_{20:1}$ ), behenic acid ( $C_{22:0}$ ), erucic acid ( $C_{22:1}$ ), brassidic acid ( $C_{22:1}$ ), etc. can be raised. These fatty acid may be used independently, or even if it uses it as mixed fatty acid of arbitrary rates, it is put, and it does not have a cane. Myristic acid, pulmitic acid, stearic acid, oleic acid, linolic acid, etc. are [ among these ] preferred.

[0023]What is necessary is just to use technology, such as a chemosynthesis method, an ester interchange method, or an extraction method from a natural product, in order to manufacture mixed triglyceride concerning above mentioned this invention which comprises long chain polyunsaturated fatty acid and fatty acid other than this n-3 system. As a chemosynthesis method, a desired quantity and fatty acid of a presentation, a fatty acid anhydride or a fatty acid halogenide (fatty acid chloride), and glycerin, for example, acid (chloride, sulfuric acid, Para toluenesulfonic acid, etc.) and an alkaline substance (sodium hydroxide.) Under existence of the esterification catalyst of metal (zinc, tin, titanium, nickel, etc.), such as a potassium hydrate, metallic oxides (a zinc oxide, alumina, ferrous oxide, etc.), metal halogenides (an aluminium chloride, tin chloride, etc.), etc., or nonexistence, It is good to carry out an esterification reaction for 1 to 25 hours, heating at 100-250 °C in a nitrogen gas air current, and removing the water to generate.

[0024]An esterification product if needed Alkali deoxidation treatment, activated carbon, the activated clay, The adsorption and fractionation processing using alumina, silica gel, ion-exchange resin, etc., Perform solvent separation processing using oleophilic organic solvents, such as a hydrophilic organic solvent and/or n-hexane, such as methanol and ethanol, and xylene, and Free fatty acid, Impurities, such as monoglyceride, diglyceride, a coloring substance, and an owner smell ingredient, are removed, The content of the n-3 system long chain polyunsaturated-fatty-acid residue which furthermore combines these processings

suitably and is combined with the 2nd place of triglyceride, it becomes less than [ of the total content of the n-3 system long chain polyunsaturated-fatty-acid residue combined with the 1st place of triglyceride, the 2nd place, and the 3rd place / 40 mol % ] -- as -- a triglyceride ingredient -- fractionation -- or it may condense. As for mixed triglyceride concerning this invention, it is desirable to blow and carry out deodorization treatment of the steam, for example under heating and decompression.

[0025]In order to obtain mixed triglyceride applied to this invention using an ester interchange method, For example, they are [ whether long chain polyunsaturated fatty acid is substantially included n-3 system with triglyceride (ingredient a-1) of fatty acid which contains long chain polyunsaturated fatty acid so much n-3 system as a raw material, and / a little ] fatty acid (ingredient a-2) of content, and low-grade alcohol ester (methyl ester, ethyl ester, etc.) of the ingredient a-2. It is the same as that of the following. Or triglyceride of the ingredient a-2 is mixed at a request rate, Or requirements mixing of the low-grade alcohol ester of triglyceride (ingredient b-1) of fatty acid of content, fatty acid (ingredient b-2) which contains long chain polyunsaturated fatty acid so much n-3 system, or the ingredient b-2 is carried out in small quantities n-3 system, excluding long chain polyunsaturated fatty acid substantially, As a catalyst, alkaline substances, such as sodium hydroxide and a potassium hydrate, It is simple to make an ester exchange reaction perform using ion-exchange resin, such as metal alcoholates (metal alkoxide), such as sodium methylate, sodium ethylate, and lithium butyrate, basic anion exchange resin, and acid cation exchange resin, or lipase. When an ester interchange is carried out using lipase specific as a catalyst, it is desirable as a method of manufacturing the 1st place and mixed triglyceride which can introduce a new fatty acid group into the 3rd place selectively, and is applied to this invention of triglyceride so that it may mention later.

[0026]The raw material of said ester interchange as the ingredient a-1 The linseed oil, sesame oil, Fish oil, such as vegetable oil, such as a beefsteak plant oil, sardine oil, cod liver oil, herring oil, a cuttlefish oil, and a tuna eye socket oil, Squeezing or extracted oil obtained considering marine mammals, such as a whale, a seal, and a fur seal, as the origin, Again milk fat of this animal, chlorella, Spirulina, Dunaliella, etc. The Nannochloropsis group (for example, Nannochloropsis oculata), a truss -- an ibis -- a thorium group (for example, Thraustochytrium aureum). The Crypthecodinium group (for example, Crypthecodinium cohnii), The fats and oils extracted from the minute alga belonging to the Isochrysis group (for example, Isochrysis galbana) etc., Triglyceride of mixed fatty acid with the fats and oils originating in microorganisms, such as the Mortierella (Mortierella) group, and said various fatty acid (refer to the clause of the paragraph number 0022) which contains long chain polyunsaturated fatty acid or this at an arbitrary rate n-3 system can be used. As the ingredient a-2, various fatty acid of a description or the derivative of those can be used for the clause of the paragraph

number 0022.

[0027]There is triglyceride obtained from animals and plants, a microorganism, minute alga, etc. as the ingredient b-1, Soybean oil, oleum rapae, cottonseed cake oil, corn oil, palm oil, palm oil, safflower oil, HAIO laic safflower oil, sunflower oil, HAIO laic sunflower oil, Olive oil, peanut oil, cacao oil, Chinese TAROU, SAL fat, Xia fat, Beef tallow, lard, these hydrogenated fats and oils, judgment fats and oils, triglyceride of said ingredient a-2, medium-chain-fatty-acid triglyceride, etc. can be illustrated, and there is fatty acid obtained by the hydrolysis treatment of said ingredient a-1 as the ingredient b-2.

[0028]As an example, an ester exchange reaction mixes said raw material so that it may be set to ingredient a-1:ingredient a-2=1:0.1 - 5, and ingredient b-1:ingredient b-2=1:2 - 10 by mole fraction, In making alkali or metal alcoholate into a catalyst, it carries out an ester exchange reaction at 80-120 °C as non-aqueous phase substantially for 0.5 to 3 hours. When using ion-exchange resin, a raw material is similarly made into non-aqueous phase, but it is good to carry out circulation contact of the raw material by a column system about room temperature -40 °C. In using lipase as a catalyst, it carries out a moisture content in a raw material to 1 or less weight %, Fixed lipase which fixed commercial lipase powder or this in diatomite, publicly known carrier, for example, cerite, activated carbon, porous glass, ion-exchange resin, chitosan, polymer gel, cellulose powder, etc. is added, and an ester exchange reaction is carried out at 20-80 °C for 0.5 to 20 hours.

[0029]Lipase can use a thing which makes the origin a microorganism described below, or a thing of animal organ origin. Namely, an Aspergillus (for example, Aspergillus niger), A Mucor (for example, Mucor miehei), the Candida group (for example, Candida cylindracea), Pseudomonas (for example, Pseudomonas fragi), Alcaligenes (for example, Alcaligenes sp. given in JP,S58-36953,B), They are pancreatic lipases belonging to Rhizopus (for example, Rhizopus delemar), the Geotrichum group (for example, Geotrichum candidum), etc., such as lipase of a microbial origin, and a swine. Among these, the 1st place of glyceride, and in order to act on the 3rd place specifically, lipase which makes the origin a microorganism of an Aspergillus, a Mucor, Alcaligenes, and Rhizopus, and swine pancreas-origin lipase are faced manufacturing mixed triglyceride concerning this invention, and are preferred.

[0030]Although the ester exchange reaction thing obtained by the various ester interchange methods mentioned above can be used as the mixed triglyceride which uses the ester exchange reaction thing itself by this invention depending on the kind of raw material to choose, Like the case of the esterification product acquired by said chemosynthesis method, If needed, it gives combining suitably alkali deoxidation treatment, adsorption and fractionation processing, solvent separation processing, or non-solvent separation (wintering) processing, and an impurity can be removed or a glyceride ingredient can also be used as fractionation or the mixed triglyceride which is condensed and is used by this invention. As for this triglyceride,



it is desirable to carry out deodorization treatment.

[0031]Mixed triglyceride concerning this invention can be obtained also by the method of extracting oil and fat content from a natural product. Namely, the inside of what was indicated as a raw material (ingredient a-1) of said ester interchange, A whale, a seal (harbour seal, harp seal, etc.), The body tissue of marine mammals, such as a fur seal, the milk secreted from this animal, The cells or these cultured cells of minute alga, such as chlorella, Spirulina, and Dunaliella, the Nannochloropsis (Nannochloropsis) group and a truss -- an ibis -- a thorium (Thraustochytrium) group. (The minute alga, for example, Nannochloropsis, belonging to the Cryptocodinium (Cryptocodinium) group, the Isochrysis (Isochrysis) group, etc. OKYU rata (Nannochloropsis oculata)) a truss -- an ibis -- thorium [ AUREUMU (Thraustochytrium aureum) and ] Cryptocodinium Cohnii (Cryptocodinium cohnii), Isochrysis Let cells or these cultured cells, such as GARUBANA (Isochrysis galbana), be raw materials. It will not interfere, if the triglyceride obtained from this satisfies the glyceride structure of this invention when making a microorganism into the origin.

[0032]These Compression treatment or n-hexane, chloroform, benzene, using organic solvents, such as diethylether and methanol, -- extracting processing -- or fractionation treatment being carried out, and oil being obtained and, A degumming, alkali deoxidation, decolorization, deodorization, etc. can be processed to this, and a glyceride fraction can be obtained except for impurities, such as free fatty acid, phospholipid, a glycolipid, an unsaponifiable matter, a coloring substance, and an owner smell ingredient. Although this glyceride fraction can be used as mixed triglyceride used by this invention, A thing which carry out fractionation of this glyceride fraction further with non-solvent low-temperature judgment, solvent separation, or a silica gel column, and combines with the 2nd place of triglyceride and for which a long chain polyunsaturated-fatty-acid residue manufactures still less triglyceride n-3 system is also possible.

[0033]Mixed triglyceride concerning this invention manufactured by a chemosynthesis method, an ester interchange method, or an extraction method from a natural product etc. which was described above, Although less than [ of a total amount of long chain polyunsaturated fatty acid / 40 mol % ] carries out an ester bond to the 2nd place of triglyceride n-3 system as the constituent fatty acids, it is less than [ 20 mol % ] more preferably. If it becomes more than 40 mol %, an effect of a request of this invention will become small. it can mix with animals-and-plants system fats and oils which it comes out of as it is, and can be used as fats and oils, and were indicated as usual edible oil and fat b-1, for example, ingredient, and mixed triglyceride concerning this invention can be used also as fats and oils. 5 to 100weight % of the whole fats and oils of content of mixed triglyceride which takes for this invention at this time are desirable, and its further 10 to 100 weight % is much more preferred. It is 20 to 100 weight % most preferably. At less than 5 weight %, an effect of a request of this invention is small.

[0034]In the triglyceride which comprises fats and oils, i.e., the fatty acid which contains long chain polyunsaturated fatty acid n-3 system, prepared by the above-mentioned method, and glycerin in this invention, Arbitrary fatty acid other than long chain polyunsaturated fatty acid is distributed over the 2nd place of triglyceride n-3 system n-3 system with less than [ of the total amount of long chain polyunsaturated fatty acid / 40 mol % ], And the fats and oils which consist of mixed triglyceride which arbitrary fatty acid other than long chain polyunsaturated fatty acid was distributed [ n-3 system ] at random or un-at random in the 1st place of triglyceride, and the 3rd place n-3 system with more than 60 mol % of the total amount of long chain polyunsaturated fatty acid, and carried out the ester bond, respectively, Or the medical-application fats-and-oils containing composition which blended the fats and oils which blend this mixed triglyceride and said arbitrary edible animal-and-vegetable-oils fat so that the content of this mixed triglyceride may be 5 weight % or more as an essential ingredient is provided.

[0035]Since polyunsaturated fatty acid is contained, except for a use like the frying oil which performs prolonged heat-treatment, the fats and oils concerning this invention can be dealt with almost like usual edible oil and fat, and can be processed with other foodstuffs raw materials. It does not interfere, even if it blends a proper quantity of tocopherol, ascorbic acid ester (palmitate, stearate, etc.), beta-carotene, and other anti-oxidants, in order to avoid quality degradation.

[0036]As a medical-application fats-and-oils containing composition as used in the field of this invention, Capsules, such as a soft capsule and a microcapsule, the drink which adjusted viscosity etc. for disease patients, Oral foods of jelly, a pudding, Cookie, ice cream, etc., simple liquid food, Common liquid food and 3-minute rice porridge, half-a-sum rice porridge which are used by taking orally, such as protein addition foods and maintenance liquid food, Blender foods of 7-minute rice porridge, all the rice porridge, etc., mixer foods, a natural high density liquid diet, an artificial high density liquid diet, Intubation high density liquid diets, such as a mixed high density liquid diet, the nature liquid food of low protein, low cholesterol liquid food, These can be taken in or prescribed for the patient for various foods for medical use and pharmaceutical preparation including the infusion-of-nutrient agent and lipid microsphere which are prescribed for the patient from taking orally thru/or intubation special liquid food, a elemental diet, and veins, such as low sodium flux foods. As a fats-and-oils containing composition concerning this invention, unless it deviates from the meaning of this invention besides the aforementioned thing, it may be used with what kind of form.

[0037]About the content of the fats and oils concerning this invention in these medical-application fats-and-oils containing composition. Although the conditions etc. which are taken in or prescribed for the patient are hard to prescribe the difference in the kind of this constituent, or a form, and it uniformly, as opposed to the whole fats and oils which are

contained in this constituent or are added -- as said mixed triglyceride -- in general -- it is 20 to 100 weight % still more preferably ten to 100weight % preferably 5weight % or more. What is necessary is just to use suitably the fats and oils (namely, fats and oils which contain the fats and oils which consist only of said mixed triglyceride, and said mixed triglyceride 5weight % or more) applied to this invention so that it may become such a blending ratio. At least one effect becomes small by said less than lower limit among the reduction effect of a blood cholesterol level and/or the triglyceride value in blood, and the depressor effect of a platelet aggregation activity. What is necessary is, to oil-in-water-type-emulsify especially the method of blending the fats and oils concerning this invention with the medical-application fats-and-oils containing composition of this invention, to water-in-oil-type-emulsify it, and it to dissolve, or to solubilize [ not to limit it, but ] it under the same operation as the time of common edible oil and fat, a procedure, and conditions, and just to make it blend with a medical-application fats-and-oils containing composition. [ mixing and ]

[0038]In the case of oral foods or liquid food, a thing various type can be prepared among the medical-application fats-and-oils containing compositions of this invention using the fats and oils concerning above publicly known food-grade raw materials and this inventions. Add the fats and oils which take for this invention at this food-grade raw material at this time, or all or a part of oil and fat content of this food-grade raw material is transposed to the fats and oils concerning this invention, What is necessary is just to make it the content of the mixed triglyceride applied to this invention to oral foods or the whole liquid food be 1 to 80 weight % preferably 0.1weight % or more. At less than 0.1 weight %, a desired effect is not expectable. Said upper limit can be suitably set up within the limits of well-known in accordance with each kind of oral foods or liquid food. In the case of the infusion-of-nutrient agent and lipid microsphere which are prescribed for the patient from a vein, As an emulsifier the fats and oils concerning purified water and this invention Lecithin of the origin, such as a soybean and an egg yolk, lysolecithins and these fractions (phosphatidylcholine and phosphatidylethanolamine.) phosphatidylinositols and these RIZO objects, and the derivative (phosphatidyl ethanol.) for which the base portion of lecithin was exchanged by the alcohol group Phosphatidylglycerol etc. are made to distribute, emulsify or solubilize using Tween 80 etc., and it can prepare, and is made for the content of the mixed triglyceride which takes for this invention to said whole pharmaceutical preparation at this time to be 1 to 30 weight % preferably 0.1weight % or more.

[0039]A blood cholesterol level and/or the triglyceride value in blood can be reduced, and a platelet aggregation activity can be made to control by taken in or prescribing the medical-application fats-and-oils containing composition of this invention for the patient. and since it is notably large compared with the case where the conventional fish oil etc. which are long chain polyunsaturated-fatty-acid supply sources n-3 system are blended, these effects are accepted

also by a little use. Based on said both effects, use for uses, such as prevention and the therapy of hyperlipidemia, prevention of arteriosclerosis, a therapy, is still more possible for the medical-application fats-and-oils containing composition of this invention.

[0040]

[Working example]

1 kg of reference example 1 trioleins, and the fish oil hydrolysis fatty acid concentrate which carried out low-temperature judgment of the fish oil (Tama Biochemical Co., Ltd. make, trade name:EPA-18) hydrolysis mixing fatty acid ( $C_{20:5}$ :37.4-mol % [ in total fatty acid ], and  $C_{22:5}$ :5.4-mol %, and  $C_{22:6}$ :25.2-mol %.) It is 72.5-mol % as long chain polyunsaturated fatty acid n-3 system. BHT -- the 0.01 weight % addition -- Lipozyme IM after mixing by mole ratio 1:5 and adjusting moisture content to 0.2weight % 20 (trade name.) Novo The product made by NORUDISUKU, Mucor The through alternative ester exchange reaction was made to perform in the glass columns (10 cm phix60 cm) filled up with lipase of I high (Mucor miehei) origin at 40 \*\*.

[0041]After removing free fatty acid from an ester exchange reaction thing in steam distillation and rinsing treatment, The column made from stainless steel filled up with the silica gel (the Wako Pure Chem make, a trade name: WAKOGERU C100) made to permeate in n-hexane was presented, and the mixed triglyceride 720g which it is made to elute by n-hexane and is applied to this invention except for diglyceride was obtained. Each fatty acid composition of the 1st place of the total-fatty-acid presentation which constitutes this triglyceride, and glyceride and the 3rd place, and the 2nd place was searched for by GLC analysis. This result is shown in Table 1. 90-mol% of  $C_{20:5}$  which constitutes this triglyceride More than 95 mol % of  $C_{22:6}$  and 93.5-mol% of the total amount of n-3 system long chain polyunsaturated fatty acid was distributed over the 1st place of triglyceride, and the 3rd place. That is, 6.5-mol% of the total amount of long chain polyunsaturated fatty acid was distributed over the 2nd place of this triglyceride n-3 system. This triglyceride was used as the test oil of the following animal experiments.

[0042]After adding 0.1 weight % of sodium methoxide to some of this triglyceride and making a random ester exchange reaction perform at 100 \*\* under decompression, it filtered using cerite and the random ester interchange thing of this triglyceride was obtained. Said the appearance was asked for each fatty acid composition of this total-fatty-acid presentation, the 1st place and the 3rd place, and the 2nd place (refer to Table 1). 50.6-mol% of the total amount of long chain polyunsaturated fatty acid was distributed over the 2nd place of this triglyceride n-3 system. This random ester interchange thing was used as the contrast oil of an animal experiment.

[0043]

[Table 1]

表1 試験油および対照油の脂肪酸組成

(単位：モル%)

脂肪酸の 種 類※	試 験 油			対 照 油		
	全体	1,3位	2位	全体	1,3位	2位
18 : 1	43	26	74	46	42	43
18 : 4 (n-3)	3	5	0	3	2	3
20 : 4 (n-3)	3	4	0	2	2	2
20 : 5 (n-3)	25	34	4	24	21	23
22 : 5 (n-3)	3	5	0	3	2	3
22 : 6 (n-3)	17	24	1	17	17	14

\* Total carbon number : display with the number of double bonds. (n-3) shows fatty acid n-3 system.

[0044]Seven 4-week old SD system male rats were made into one experimental plot, and the rearing experiment was conducted using the feed (refer to Table 2) which blended test oil and a contrast oil 5weight % each. In order to prevent the oxidation degradation of feed ingredients in the meantime, feed was prepared every day and fed. After carrying out free ingestion of water and said each feed and breeding them for three weeks, neutral lipid [ in the blood of each experimental plot rat and liver ], total cholesterol, and phospholipid each content was measured. This result is shown in Table 3. The amount of each of  $\text{PGI}_2$  of the main artery of each experimental plot rat and  $\text{TXA}_2$  in blood was measured simultaneously. This result is shown in Table 4. As for the significant difference, each experimental plot was not observed in the amount of feed intake, body weight gain, and pancreas weight.

[0045]The fats and oils (test oil) which consist of mixed triglyceride concerning this invention do not have side effects to a rat, and it became clear from this experimental result that triglyceride in blood (neutral lipid) and the value of total cholesterol, and the value of triglyceride in liver decrease notably in the division which added test oil. In the division which added the fats and oils (test oil) which consist of mixed triglyceride concerning this invention. It became clear that the production amount of  $\text{PGI}_2$  increases notably (namely, increase in the depressant action of a platelet aggregation activity and an artery relaxation operation), and the production amount of  $\text{TXA}_2$  decreases extremely (namely, fall of an induction operation of a platelet aggregation activity and an arteriartia operation). Therefore, a possibility that the fats and oils which consist of mixed triglyceride concerning this invention could be used for prevention of hyperlipidemia or arteriosclerosis and a therapy was realized.

[0046]

[Table 2]

表2 飼料組成  
(単位：重量%)

コーンスターチ	41.7
カゼイン	20.0
デキストリン	13.2
シュクロース	10.0
脂肪（試験油または対照油）	5.0
セルロース粉末	5.0
ミネラルミックス（※1）	3.5
ビタミンミックス（※2）	1.0
Ｌ－シスチン	0.3
重酒石酸コリン	0.2
TBHQ（※3）	0.1

\*\*1 The CLEA Japan, Inc. make, AIN-93 G-MX \*2 CLEA Japan, Inc. make, AIN-93-VX \*3 t-butylhydroquinone[0047]

[Table 3]

表3 血漿および肝臓中脂質濃度

	試験油添加区	対照油添加区
血漿脂質(mg/dl)		
トリグリセリド	130 ± 4 ※	230 ± 7
総コレステロール	123 ± 4 ※	155 ± 5
リン脂質	92 ± 3 ※	125 ± 4
肝臓脂質(mg/g-liver)		
トリグリセリド	10.5 ± 0.3 ※	17.0 ± 0.5
総コレステロール	2.5 ± 0.1	3.5 ± 0.1
リン脂質	29.3 ± 0.9	31.6 ± 1.1

\* To the value of a contrast oil additive area, it is 5% or less of percentage of risk, and they are those with a significant difference.

[0048]

[Table 4]

表4 PGI<sub>2</sub> およびTXA<sub>2</sub> 濃度

	試験油添加区	対照油添加区
PGI <sub>2</sub> (pg/mg-aorta)	3 0 3 ± 9 ※	1 2 2 ± 4
TXA <sub>2</sub> (ng/ml)	2 9 4 ± 8 ※	5 5 6 ± 1 7

\* : it is the same as notes of Table 3.

[0049]Reference example 2 test-oil fat (fats and oils containing mixed triglyceride of this invention) and contrast fats and oils were prepared as follows. That is, test oil fat is dry ice / acetone refrigerant, cooled -80 \*\* of harp seal (seal) fats and oils for 1 hour, and filtered and prepared the crystal part which deposited through the filter paper. Contrast fats and oils shall blend the concentrate which cooled similarly [ in dry ice / acetone refrigerant ] two kinds of fish oil (the mixed oil of the cod liver oil and a small fish oil, a tuna eye socket oil) in which fatty acid composition differs, and was classified, and shall approximate the total-fatty-acid presentation mostly with it of test oil fat. Such fatty acid composition is shown in Table 5.

[0050]

[Table 5]

表5 試験油脂および対照油脂の脂肪酸組成  
(単位：モル%)

脂肪酸の種類※	試 験 油 脂			対 照 油 脂		
	全体	1,3位	2位	全体	1,3位	2位
16:0	2	1	3	9	11	7
16:1	16	7	32	9	10	6
18:0	0	0	0	2	3	0
18:1	14	12	18	16	20	8
18:2	3	0	6	1	2	1
18:3 (n-3)	2	0	4	1	1	1
18:4 (n-3)	6	6	5	4	4	5
20:1	4	6	1	3	4	2
20:4 (n-3)	2	2	1	3	3	3
20:5 (n-3)	14	21	3	19	15	25
22:1	1	1	0	2	1	1
22:5 (n-3)	7	10	1	2	1	3
22:6 (n-3)	19	28	3	19	14	27

\* : it is the same as notes of Table 1.

[0051]Fats and oils which make seven 4-week old SD system male rats one experimental plot, and contain aforementioned test oil fat and contrast fats and oils 20weight %, respectively (mixed fats and oils of test oil fat or contrast fats-and-oils 20 weight section, palm oil 50 weight section, HAO laic safflower oil 5 weight section, and high-linoleic-safflower-oil 25 weight section.) Fatty acid composition is referring to Table 6. It is the feed (a feed presentation is the same as the reference example 1 except making 5 weight % of fats into 10 weight %, and making 41.7 weight % of cornstarch into 36.7 weight %.) blended 10weight % each, and the rearing experiment was conducted. In order to prevent the oxidation degradation of feed ingredients in the meantime, feed was prepared every day and fed. After carrying out free ingestion of water and said each feed and breeding them for three weeks, neutral lipid [ in the blood of each experimental plot rat and liver ], total cholesterol, and phospholipid each content was measured like the reference example 1 (refer to Table 7). Similarly the amount of each of  $\text{PGI}_2$  of the main artery of each experimental plot rat and  $\text{TXA}_2$  in blood was measured (refer to Table 8). The difference with each experimental plot significant in a feed amount of food ingested, body weight gain, and liver weight was not accepted.

[0052]The fats and oils (test oil fat) containing mixed triglyceride concerning this invention not doing side effects to a rat, but reducing effectively triglyceride (neutral lipid) in blood and liver and the value of total cholesterol from this experimental result, was accepted. In the division which added test oil fat, it became clear that increase of a  $\text{PGI}_2$  production amount and reduction of a  $\text{TXA}_2$  production amount, i.e., the depressant action of a platelet aggregation activity and an arterial blood pipe extension operation, are reinforced. Therefore, a possibility that the fats and oils containing mixed triglyceride concerning this invention could be used for prevention of hyperlipidemia or arteriosclerosis and a therapy was realized.

[0053]

[Table 6]



表6 飼料中油脂の脂肪酸組成

(単位：モル%)

脂肪酸の種類 ※	試 験 油 脂 20重量%配合	対 照 油 脂 20重量%配合
16:0	26.9	26.6
16:1	2.8	1.8
18:0	3.1	3.1
18:1	28.6	29.6
18:2 (n-6)	23.5	22.8
18:3 (n-3)	0.6	0.5
18:4 (n-3)	1.0	0.8
20:1	0.8	0.7
20:4 (n-3)	0.1	0.5
20:5 (n-3)	2.7	3.6
22:1	0.1	0.2
22:5 (n-3)	1.2	0.4
22:6 (n-3)	3.6	3.5
その他	5.0	5.9
脂肪酸の比率 ※※		
飽 和	34.1	34.5
モノ不飽和	33.3	33.3
n-6系	23.5	23.3
n-3系	9.1	9.0

\* : it is the same as notes of Table 1. (n-6) shows n-6 fatty acid.

\*\* : -- saturated fatty acid, mono-unsaturated fatty acid, n-6 fatty acid, and n-3 system -- fat each fatty acid of the \*\*\*\* -- comparatively .

[0054]

[Table 7]

表7 血漿および肝臓中脂質濃度

	試験油脂添加区	対照油脂添加区
血漿脂質 (mg/dl)		
トリグリセリド	1 4 5 ± 4 ※	2 2 3 ± 7
総コレステロール	1 5 4 ± 5 ※	1 7 2 ± 5
リン脂質	9 4 ± 3	1 2 1 ± 4
肝臓脂質 (mg/g-liver)		
トリグリセリド	1 1 . 6 ± 0 . 3 ※	1 6 . 0 ± 0 . 5
総コレステロール	2 . 6 ± 0 . 1	3 . 1 ± 0 . 1
リン脂質	3 1 . 2 ± 0 . 9	3 1 . 6 ± 1 . 0

\* : it is the same as notes of Table 3.

[0055]

[Table 8]

表8 PGI<sub>2</sub> およびTXA<sub>2</sub> 濃度

	試験油脂添加区	対照油脂添加区
PGI <sub>2</sub> (pg/mg-aorta)	1 8 9 ± 6 ※	1 3 7 ± 4
TXA <sub>2</sub> (ng/ml)	3 1 6 ± 9 ※	4 1 8 ± 1 3

\* : it is the same as notes of Table 3.

[0056]The fats and oils into which the blending ratio of the test oil fat used by the reference example 3 reference example 2 and contrast fats and oils was changed were added in feed, and the rat rearing experiment was conducted like the reference example 2. namely, the fats and oils (test oil fat or contrast fats and oils -- 10 weight section) which make seven 4-week old SD system male rats one experimental plot, and contain the test oil fat or contrast fats and oils of a description in the reference example 2 10weight %, respectively Mixed fats and oils of palm oil 50 weight section, HAIO laic safflower oil 10 weight section, and high-linoleic-safflower-oil 30 weight section. Fatty acid composition is referring to Table 9. It is the feed (a feed presentation is the same as the reference example 2 except for fat.) blended 10weight % each, and the rearing experiment was conducted. In order to prevent the oxidation degradation of feed ingredients in the meantime, feed was prepared every day. After carrying out free ingestion of water and said each feed and breeding them for three weeks, neutral lipid [ in the blood of each experimental plot rat and liver ], total cholesterol, and phospholipid each content was measured like the reference example 1 (refer to Table 10). Similarly the amount of each of

$\text{PGI}_2$  of the main artery of each experimental plot rat and  $\text{TXA}_2$  in blood was measured (refer to Table 11). The difference with each experimental plot significant in the amount of feed intake, body weight gain, and liver weight was not accepted.

[0057] From this experimental result and the result of the reference example 2, the fats and oils (test oil fat) containing mixed triglyceride concerning this invention do not do side effects to a rat, Having the effects also including the case of the fats and oils which mixed a little test oil fat compared with contrast fats and oils of reducing notably the value of triglyceride (neutral lipid) in blood and liver was accepted. In the division which added test oil fat, increase of a  $\text{PGI}_2$  production amount and reduction of the  $\text{TXA}_2$  production amount were caused, and it became clear to make the depressant action of a platelet aggregation activity and an extended operation of an arterial blood pipe enhance. A possibility that the fats and oils containing the mixed triglyceride applied to this invention from this could be used for prevention of hyperlipidemia or arteriosclerosis and a therapy was realized.

[0058]

[Table 9]

表 9 飼料中油脂の脂肪酸組成  
(単位：モル%)

脂肪酸の種類 ※	試 験 油 脂 10重量%配合	対 照 油 脂 10重量%配合
16:0	27.0	27.1
16:1	1.2	0.8
18:0	3.0	3.2
18:1	32.3	32.3
18:2 (n-6)	26.2	26.3
18:3 (n-3)	0.5	0.5
18:4 (n-3)	0.5	0.4
20:1	0.4	0.4
20:4 (n-3)	0.1	0.3
20:5 (n-3)	1.2	1.8
22:1	0.1	0.1
22:5 (n-3)	0.6	0.2
22:6 (n-3)	1.7	1.8
その他	5.2	4.8
脂肪酸の比率 ※※		
飽 和	33.9	33.5
モノ不飽和	34.8	34.8
n-6系	26.8	26.6
n-3系	4.6	5.1

\* And \*\* : it is the same as notes of Table 6.

[0059]

[Table 10]

表 10 血漿および肝臓中脂質濃度

	試験油脂添加区	対照油脂添加区
血漿脂質 (mg/dl)		
トリグリセリド	140 ± 4 ※	317 ± 12
総コレステロール	163 ± 5	187 ± 5
リン脂質	103 ± 3	125 ± 4
肝臓脂質 (mg/g-liver)		
トリグリセリド	12.1 ± 0.4 ※	17.2 ± 0.5
総コレステロール	2.8 ± 0.1	2.9 ± 0.1
リン脂質	30.2 ± 0.9	30.5 ± 0.9

\* : it is the same as notes of Table 3.

[0060]

[Table 11]

表 1 1      P G I<sub>2</sub> および T X A<sub>2</sub> 濃度

	試験油脂添加区	対照油脂添加区
P G I <sub>2</sub> (pg/mg-aorta)	1 7 2 ± 5 ※	1 2 4 ± 4
T X A <sub>2</sub> (ng/ml)	3 1 6 ± 1 0 ※	6 9 2 ± 2 8

\* : it is the same as notes of Table 3.

[0061]Reference example 4 minute-alga *Cryptocodinium cohnii* () [ *Cryptocodinium cohnii* and ] ATCC 30336 was planted in 30 l. of culture media shown in Table 12, at 30 \*\*, aeration culture was carried out with the jar fermenter for 100 hours, culture fronds were centrifuged and collected from culture medium, and this was freeze-dried further (yield of 625g). this dry frond -- chloroform: -- the inside of methanol =1:1 (weight ratio) mixed solvent -- HISUKO TRON (trade name.) Cell crushing was carried out by the Niton Irika Kikai Seisakusyo make, it extracted, and 520 g of oil was obtained. Presented with said oil the column made from stainless steel filled up with the silica gel (the Wako Pure Chem make, a trade name: WAKOGERU C100) distributed in n-hexane, it was made to elute in diethylether:n-hexane =10:90 (capacity factor), and the mixed triglyceride 250g concerning this invention was obtained. The fatty acid composition of this triglyceride (this was made into test oil) was searched for like the reference example 1 (refer to Table 13).

[0062]

[Table 12]

表12 培地組成  
(単位：培地1リットル中の重量)

NaCl	23.48	g
MgCl <sub>2</sub> ・6H <sub>2</sub> O	10.63	g
Na <sub>2</sub> SO <sub>4</sub>	3.92	g
CaCl <sub>2</sub>	1.11	g
HCl	0.66	g
NaHCO <sub>3</sub>	0.19	g
KBr	0.10	g
H <sub>3</sub> BO <sub>3</sub>	0.03	g
SrCl <sub>2</sub> ・6H <sub>2</sub> O	5.00	g
FeCl <sub>3</sub> ・6H <sub>2</sub> O	0.01	g
グリセロリン酸ナトリウム	0.15	g
(NH <sub>4</sub> ) <sub>2</sub> SO <sub>4</sub>	0.05	g
K <sub>2</sub> HPO <sub>4</sub>	0.01	g
トリス(ヒドロキシメチル)アミノメタン	3.00	g
グルコース	3.00	g
グルタミン酸ナトリウム	1.50	g
ビタミンミックス水溶液(※1)	1.0	ml
メタルミックス水溶液(※2)	3.0	ml

(pH: 6.8)

\*\*1: Vitamin mix solution (weight in this 1 l. of solution)

Biotin: 0.003 g Thiamin: 1.000 g \*2: Metal mix solution (weight in this 1 l. of solution)

Na<sub>2</sub>EDTA: 1.00 g FeCl<sub>3</sub> and 6H<sub>2</sub>O: 0.05 g H<sub>3</sub>BO<sub>3</sub>: 1.00 g MnCl<sub>2</sub> and 4H<sub>2</sub>O: 0.15 g ZnCl<sub>2</sub>: 0.01 g CoCl<sub>2</sub> and 6H<sub>2</sub>O: 0.005g[0063]

[Table 13]

表 1 3 試験油脂の脂肪酸組成

(単位：モル%)

脂肪酸の種類 ※	全 体	1, 3 位	2 位
1 0 : 0	4. 1	5. 7	0. 9
1 2 : 0	1 5. 2	2. 9	3 9. 9
1 4 : 0	2 2. 4	2 1. 1	2 5. 1
1 6 : 0	1 6. 9	2 3. 8	3. 0
1 8 : 0	0. 8	0. 6	1. 3
1 8 : 1	8. 7	6. 4	1 3. 4
1 8 : 2	0. 2	0. 3	0. 1
2 2 : 6 (n-3)	3 0. 9	3 8. 4	1 5. 8
その他	0. 8	0. 8	0. 5

\* : it is the same as notes of Table 1.

[0064]the fats and oils (test oil fat or contrast fats and oils -- 10 weight section) which contain the contrast fats and oils of a description in triglyceride (test oil fat) and the reference example 2 of minute alga origin which were obtained in this way 10weight %, respectively Mixed fats and oils of palm oil 50 weight section, HAO laic safflower oil 10 weight section, and high-linoleic-safflower-oil 30 weight section. Fatty acid composition prepared the feed (a feed presentation is the same as the reference example 3 except for fat.) which blended "refer to Table 14" 10weight % each, and did the same breeding examination as the reference example 3. The analysis result of the inside of the blood of each experimental plot rat and the lipid content in liver is shown in Table 15. The analysis result of the production amount of  $PGI_2$  of the main artery of each experimental plot rat and  $TXA_2$  in blood is shown in Table 16. As for the significant difference, each experimental plot was not observed in the amount of feed intake, body weight gain, and liver weight.

[0065]From this experimental result and the result of the reference example 2, the fats and oils (test oil fat) containing mixed triglyceride concerning this invention do not do side effects to a rat, Having the effects also including the case of the fats and oils which mixed a little test oil fat compared with contrast fats and oils which carry out reduction of triglyceride (neutral lipid) in blood and liver and the value of total cholesterol notably was accepted. In the division which added test oil fat, increase of a  $PGI_2$  production amount and reduction of the  $TXA_2$  production amount were caused, and it became clear to make the depressant action of a platelet aggregation activity and an extended operation of an arterial blood pipe enhance. A possibility that the fats and oils containing the mixed triglyceride applied to this invention from this could be used for prevention of hyperlipidemia or arteriosclerosis and a therapy was realized.

[0066]

[Table 14]

表 1 4      飼料中油脂の脂肪酸組成  
(単位：モル%)

脂肪酸の種類 ※	試 験 油 脂 1 0 重量%配合	対 照 油 脂 1 0 重量%配合
1 4 : 0	3 . 2	0 . 0
1 6 : 0	2 9 . 5	2 6 . 6
1 6 : 1	1 . 2	1 . 8
1 8 : 0	2 . 5	3 . 1
1 8 : 1	2 8 . 1	2 9 . 6
1 8 : 2 (n-6)	2 2 . 4	2 2 . 8
1 8 : 3 (n-3)	0 . 7	0 . 5
1 8 : 4 (n-3)	1 . 0	0 . 8
2 0 : 1	0 . 6	0 . 7
2 0 : 4 (n-3)	0 . 1	0 . 5
2 0 : 5 (n-3)	0 . 0	3 . 6
2 2 : 1	0 . 0	0 . 2
2 2 : 5 (n-3)	0 . 0	0 . 4
2 2 : 6 (n-3)	3 . 6	3 . 5
その他	7 . 1	5 . 9
脂肪酸の比率 ※※		
飽 和	3 8 . 4	3 4 . 5
モノ不飽和	3 1 . 9	3 3 . 3
n - 6 系	2 3 . 9	2 3 . 3
n - 3 系	5 . 8	9 . 0

\* And \*\* : it is the same as notes of Table 6.

[0067]

[Table 15]



表 1 5 血漿および肝臓中脂質濃度

	試験油脂添加区	対照油脂添加区
血漿脂質(mg/dl)		
トリグリセリド	1 3 4 ± 4 ※	2 3 3 ± 7
総コレステロール	1 3 5 ± 5 ※	1 6 7 ± 5
リン脂質	9 4 ± 4 ※	1 2 5 ± 5
肝臓脂質(mg/g-liver)		
トリグリセリド	9. 2 ± 0. 3 ※	1 6. 4 ± 0. 5
総コレステロール	2. 5 ± 0. 1	3. 3 ± 0. 1
リン脂質	2 9. 7 ± 0. 8	3 0. 8 ± 0. 8

\* : it is the same as notes of Table 3.

[0068]

[Table 16]

表 1 6 P G I<sub>2</sub> および T X A<sub>2</sub> 産生量

	試験油脂添加区	対照油脂添加区
P G I <sub>2</sub> (pg/mg-aorta)	2 0 2 ± 8 ※	1 2 5 ± 5
T X A <sub>2</sub> (ng/ml)	3 0 7 ± 1 2 ※	5 2 4 ± 1 9

\* : it is the same as notes of Table 3.

[0069]Any 3 weight sections of the fats and oils (reference example 1: fats and oils which contain test oil, the fats and oils which contain reference example 2:test oil fat 20weight %, the reference example 3, and 4:test oil fat 10weight %) concerning this invention prepared by the working example 1 reference examples 1-4, a soybean lecithin (the Nisshin Oil Mills [, Ltd. ] make, a trade name: basis LP gas-20.) It is below the same. After mixing 0.2 weight section and egg white 10 weight section and fully stirring, cow's milk 180 warmed weight section was added, it stirred for 2 minutes, and fats-and-oils content cow's milk was obtained. These things were energy 148Kcal, the protein 6.6g, 9.3 g of lipid, and the sugar 8.7g, and were liquid food which does not have a problem in flavor and appearance in any way as a result of evaluation by flavor and ten special panels.

[0070]After mixing well any 1.5 weight sections of the fats and oils (refer to working example 1) concerning this invention prepared by the working example 2 reference examples 1-4, soybean lecithin 0.1 weight section, and whole egg 20 weight section, cow's milk 60 weight section was added and it stirred enough [ further ]. This was slushed into the small cup, it

steamed for about 20 minutes over low heat, and the fats-and-oils content pudding was obtained. These things were energy 104Kcal, the protein 4.4g, 5.8 g of lipid, and the sugar 8.1g, and as a result of estimating it as working example 1 similarly, they were liquid food which does not have what problems in flavor and appearance.

[0071]Any 20 weight sections of the fats and oils (refer to working example 1) concerning this invention prepared by the working example 3 reference examples 1-4, Medium-chain-fatty-acid triglyceride (Nisshin Oil Mills, Ltd. make, trade name:ODO) 10 weight section, Egg white 10 weight section, casein (New Zealand daily board company make, trade name:Alacid) 10 weight section, dextrin (Matsutani Chemical Industry [ Co., Ltd. ] make trade name: Glyster P) 50 weight section, and water 100 weight section were fully stirred, and the high density liquid diet was obtained. These things were energy 519Kcal, the protein 9.6g, 30.2 g of lipid, and the sugar 50.1g, and as a result of estimating it as working example 1 similarly, they were liquid food which does not have what problems in flavor and appearance.

[0072]It applied to fire, melting and mixing fats-and-oils (refer to working example 1) 8 weight section, cornstarch 83 weight section, and salt 3 weight section concerning this invention prepared by the working example 4 reference example 3 with lukewarm water, the sediment was lost, and fire was stopped in the place where it gelatinized white. After becoming about 50 \*\*, diastase 6 weight section was added, and it was neglected for a while. What furthermore swelled rice flour 44 weight section with water to this, skim milk 44 weight section, It adds, respectively, and the thing which mixed and melted sugar 35 weight section and powder vegetable 10 weight section, and the thing which could boil respectively beef liver 22 weight section and \*\*\*\* (what was taken down to three sheets) 44 weight section with soy sauce, and mashed them are often melted, is mixed, and had been boiled. This was cooled to the temperature about body warmth, it strained by having added yogurt 90 weight section and hen's egg 100 weight section, and 1 l. of natural high density liquid diets were obtained. This thing was energy 1228Kcal, the protein 58.1g, 25.1 g of lipid, and the sugar 187.4g, and was liquid food which does not have what problems in flavor and appearance.

[0073]Fats-and-oils (refer to working example 1) 13 weight section concerning this invention prepared by the working example 5 reference example 1, soybean lecithin 0.8 weight section, skim milk/sugar =2 / 1 (weight ratio) mixture 96 weight section, and thick fruit-juice 45 weight section were stirred well, and were boiled up. This was cooled to the temperature about body warmth, it strained by having added hen's egg 100 weight section, and 1 l. of mixed high density liquid diets were obtained. This thing is energy 993Kcal, the protein 44.5g, 28.3 g of lipid, and sugar 140.9, and there are no what problems in flavor and appearance. What blended the fats and oils (refer to working example 1) applied to this invention prepared by the reference example 4 as fats and oils on the same method and conditions as the above, the thing which blended preparation vegetable oil, the thing which blended the contrast oil

prepared by the reference example 1, and the thing which blended the fats and oils which contain the contrast fats and oils of reference example 4 description 10weight % were prepared.

[0074]Using five sorts of these liquid food as examination feed, seven 4-week old SD system male rats were made into one experimental plot, and the free food intake was carried out for three weeks. The difference with each experimental plot significant in the amount of feed intake, body weight gain, and liver weight was not accepted. The result of having measured the lipid concentration in blood, and the amount of eicosanoid production like the reference example 1, When the fats and oils concerning this invention were blended, all, compared with the case where preparation vegetable oil and contrast fats and oils are blended, the reduction degree of a blood cholesterol level and the triglyceride value in blood is large, and there are many production amounts of  $\text{PGI}_2$ , and there were few production amounts of  $\text{TXA}_2$  again.

[0075]After stirring with a homogenizer 12000 rpm of fats-and-oils (refer to working example 1) 10 weight sections and soybean lecithin 1.2 weight sections concerning this invention prepared by the working example 6 reference example 1 for 15 minutes, Glycerin 2.5 weight section and distilled water 90 weight section are added, further, with the homogenizer, it stirred for 20 minutes and preliminary emulsification of the 20000 rpm was carried out. It is an French press (trade name.) about preliminary emulsification liquid. Using the product made by Aminco, it processed 5 times by the pressure of 638 psi, and lipid microsphere was obtained. It is coal tar N4 counter (trade name.) about the particle diameter of this lipid microsphere. When measured by the department machine company make of a day, it was  $200 \times 25$  nm. Although it observed at  $4 \times$  and particle diameter measurement and an emulsified state were observed for this lipid microsphere under naked-eye view and a polarization microscope after one-month or more preservation at six months and  $40 \times$  with the room temperature for six months, change was not accepted but was maintaining the good emulsified state. It replaced with said fats and oils, and the fat emulsifier was similarly prepared using the contrast oil of reference example 1 description.

[0076]Five 4-week old SD system male rats are made into one experimental plot by considering lipid microsphere which blended said contrast oil as control, The result of having measured the lipid concentration in blood and the amount of eicosanoid production of 4 hours after after prescribing each lipid microsphere for the patient from a caudal vein every [ 500micro / l ], When the lipid microsphere which blended the fats and oils concerning this invention was prescribed for the patient, compared with control, the reduction degree of the blood cholesterol level and the triglyceride value in blood was large, there were many  $\text{PGI}_2$  production amounts, and there were few production amounts of  $\text{TXA}_2$ .

[0077]Lipid microsphere was prepared by the method indicated in working example 6 using

fats-and-oils (refer to working example 1) 10 weight section concerning this invention prepared by the working example 7 reference example 4, yolk lecithin (Funakoshi Co., Ltd. make, reagent grade) 3.6 weight section, glycerin 30 weight section, and distilled water 70 weight section. The particle diameter measured like the example was 63\*\*18 nm. Although particle diameter measurement and an emulsified state were observed for this lipid microsphere under naked-eye view and a polarization microscope after preservation for 4 \*\* six-month and room temperature six months and, and 40 \*\* more than one month, change was not accepted but was maintaining the good emulsified state.

[0078]Lipid microsphere which prepared the contrast fats and oils of the description similarly using the fats and oils included 10weight % to the reference example 4 is considered as control, What made five 4-week old SD system male rats one experimental plot, and mixed lipid microsphere and a physiological saline by the weight ratio 1:1, When the lipid microsphere which blended the fats and oils concerning this invention as a result of measuring the lipid concentration in blood and the amount of eicosanoid production of 4 hours after is prescribed for the patient after prescribing a medicine for the patient from a caudal vein every [ 700micro / l ], Compared with control, the reduction degree of the blood cholesterol level and the triglyceride value in blood was large, there were many PGI<sub>2</sub> production amounts, and there were few production amounts of TXA<sub>2</sub>.

[0079]

[Effect of the Invention]The medical-application fats-and-oils containing composition of this invention does not have side effects to an animal including Homo sapiens, The effect which carries out reduction of a blood cholesterol level and/or the triglyceride value in blood compared with the conventional thing which blended the long chain polyunsaturated-fatty-acid supply source n-3 system is large, And it is large, the effect, i.e., the platelet aggregation activity depressor effect, which are made to increase the PGI<sub>2</sub> production amount of eicosanoid, and make a TXA<sub>2</sub> production amount decrease. For this reason, rather than the conventional things which blended the long chain polyunsaturated-fatty-acid supply source n-3 system, such as fish oil, the fats-and-oils containing composition of this invention can improve the lipid concentration in blood, and can control and adjust an aggregation of blood platelets by a little ingestion, and it becomes possible to use for the use of prevention of hyperlipidemia or arteriosclerosis, and a therapy.

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[Translation done.]